Relation of oropharyngeal palsy to neck and limb weakness in Guillain-Barré and Fisher's syndromes

	Oropharyngeal palsy				
	Present (n=48)	Absent (n=104)	p Value	Odds ratio	95% CI
Ophthalmoplegia	18 (38%)	35 (34%)	0.6		
Neck weakness	36 (75%)	33 (32%)	<0.0001	6.5	3.1–13.6
Arm dominant weakness	20 (42%)	13 (13%)	<0.0001	5.0	2.3–10.9
Leg dominant weakness	11 (23%)	50 (48%)	0.003	0.3	0.1–0.7

Differences in proportions were examined by χ^2 test. 95%CI=95% confidence interval.

only in patients who have a restricted distribution of muscle weakness in the pharynx, neck, and proximal upper limbs but no weakness or areflexia in the legs. In his original report,[2] however, one of the three patients with PCB had generalised areflexia. Moreover, the patient with Guillain-Barré syndrome described by Mizoguchi *et al*,[3] whose initial symptoms were lower cranial nerve dysfunction and upper limb weakness, later developed generalised muscle weakness. These patients with PCB with generalised areflexia or weakness indicate that the preservation of the tendon reflex and muscle power in the legs depends on the severity of the involvement of the limbs. None of the patients in our study met the clinical criteria proposed by Ropper.[1] However, the close association of weakness of the pharynx, neck, and upper limbs in Guillain-Barré syndrome and Fisher's syndrome indicates that PCB is a distinct variant of Guillain-Barré syndrome, because ophthalmoplegia, a cardinal sign in Fisher's syndrome, is not associated with oropharyngeal palsy, neck weakness, or arm dominant weakness.

Our finding is also supported by detection of serum antibodies against GT1a ganglioside in patients with PCB which show different reactivity from those in patients with Fisher's syndrome.[3 4] IgG anti-GT1a antibodies in patients with PCB are not absorbed by GQ1b ganglioside whereas those in patients with Fisher's syndrome are.[4] Because only GT1a is recognised by serum IgG from the patient who had a restricted distribution of muscle weakness in the pharynx, neck, and proximal upper limbs,[4] we speculate that anti-GT1a and anti-GD1a antibodies respectively contributed to the development of PCB and generalised weakness in the patient described by Mizoguchi *et al*.[3]

MICHIAKI KOGA
NOBUHIRO YUKI
KOICHI HIRATA
Department of Neurology, Dokkyo University School of Medicine, Tochigi, Japan

Correspondence to: Dr Michiaki Koga, Department of Neurology, Dokkyo University School of Medicine, Kitakobayashi 880, Mibu, Shimotsuga, Tochigi 321–0293, Japan. Tel: 0081 282 86 1111 extention 2733 or 2578; fax 0081 10-60-89313; email: koga@dokkyomed.ac.jp

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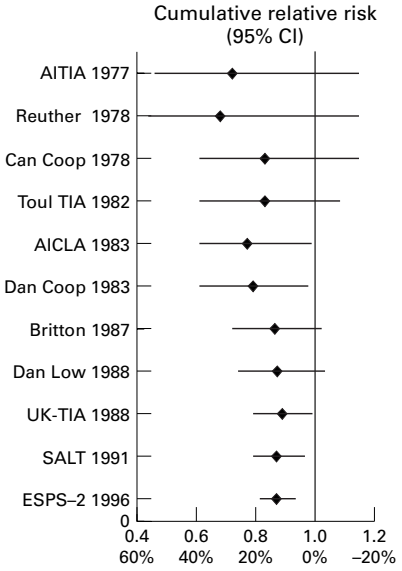
Cumulative meta-analysis of aspirin efficacy after cerebral ischaemia of arterial origin

In 1996 we reported in this *Journal* that there was virtually no difference in relative risk reduction for low (<100 mg/day), medium (300 to 325 mg/day), and high (>900 mg/day) doses of aspirin in the prevention of vascular events in patients with cerebral ischaemia of arterial origin.[1] A meta-analysis of the cumulative data showed a modest 13% (95% confidence interval (95% CI) 4% to 21%) relative risk reduction. Recently the final data of the second European Stroke Prevention Study (ESPS-2) were reported.[2] One of its comparisons was between 50 mg aspirin daily and placebo in patients after cerebral ischaemia; the relative risk reduction of 13% (95% CI 0% to 24%) was exactly the same as that resulting from our previous meta-analysis. This similarity allows the calculation of an update of the meta-analysis. The overall relative risk reduction of course remains 13%, but the 95% CI has narrowed to 6% to 19%. The figure shows the results of the updated cumulative meta-analysis, in chronological order. These data once more underscore the need for more efficacious treatment strategies. For this reason we started the European and Australian Stroke Prevention in Reversible Ischaemia Trial (ESPRIT).[3]

A ALGRA
J VAN GIJN
Julius Center for Patient-Orientated Research, and University Department of Neurology, Utrecht, The Netherlands

Correspondence to: Dr Ale Algra, Julius Center for Patient-Orientated Research, University Hospital Utrecht, P O Box 85500, 3508 GA Utrecht, The Netherlands. Telephone 0031 30 250 9350; fax 0031 30 250 5485; email A.Algra@neuro.azu.nl



Cumulative meta-analysis in chronological order (1977 to 1996) with relative risks and corresponding relative risk reductions with 95% CIs. Each line represents the relative risk and 95% CI of that study combined with all previous studies.

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CORRESPONDENCE

Hemifacial spasm

We have looked with interest at the scan of a patient with hemifacial spasm by Reigosa and Rios.[1] Indeed, this is a very nice MRI which shows an arterial loop and the internal auditory meatus. However, this loop is not the cause of hemifacial spasm.

Typical hemifacial spasm, which begins in the orbicularis oculi and gradually progresses down the face, is caused by a blood vessel on the non-fascicular portion of the facial nerve on the caudal or anterior aspect, including the intrapontine nerve. Atypical hemifacial spasm, which starts in the buccal muscles and progresses up the face, is caused by a blood vessel on the posterior or rostral side of the nerve. This is much less common. The compression is also at the brainstem. A distal artery, as shown in the scan, does not cause hemifacial spasm. The syllogism that Reigosa and Rios bring out—namely, that botulinum toxin helped and that this picture showed the pathology, is inadequate. They do not have a completed explanation.

This patient's spasm will recur because the cause has not been treated. The spasm has an excellent chance of responding to a microvascular decompression of the facial nerve performed by a neurosurgeon who has experience in the nuances of the operative procedure.

Nevertheless, Reigosa and Rios have shown a beautiful scan.

PETER J JANNETTA
AMIN KASSAM
Department of Neurological Surgery, School of Medicine, University of Pittsburgh, PA, USA

1 Reigosa RP, Rios JP. Hemifacial spasm. *J Neurol Neurosurg Psychiatry* 1998;**64**:687.

Pego Reigosa replies:

We thank Jannetta and Kassam for their interest in our article.[1] We think that the vascular loop that appears in the MR image is indeed the cause of the hemifacial spasm of our patient, as it is the only abnormal finding of the neuroimaging studies performed. Furthermore, we did not find compression of the nerve at other levels where it is more often encountered, as is the caudal aspect of the VII cranial nerve next to the pons.

Moreover, it is evident that the hemifacial spasm will reappear or recur. For this reason,

the patient is receiving local botulinum toxin, with an excellent response. This treatment was chosen because its secondary effects are scarce and limited in time, and it is beneficial for a great proportion of patients. Also, systemic complications have not been described.[2] Undoubtly, it is a symptomatic treatment based on the blockade of neuromuscular transmision. With respect to surgery, microvascular decompression is an excellent treatment when it is performed by an experienced team,[3] although it poses potential complications and sequelae. Many patients, as in our case, are not willing to undergo such risks. For these reasons, we think that the treatment of choice in our patient is local injection of botulinum toxin.

R PEGO REIGOSA

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Measuring the rate of progression and estimating the preclinical period of Parkinson's disease with [^{18}F] dopa PET

Morrish *et al*[1] report in great detail the PET data on 32 patients with Parkinson's disease, from which they conclude that the mean preclinical period "is unlikely to be longer than 7 years". This conclusion is based on calculations using the [^{18}F] dopa influx constant (Ki) of the putamen, although they acknowledge that other methods of analysis and extrapolation yielded estimates of anything between 2.8 and 37.2 years. The authors justify using putamen Ki because it was "more sensitive to increasing disability" than either total striatal assessment or using the alternative ratio approach, but fail to justify a much more fundamental and unwise assumption on which their arguments rest—that is, the intercorrelation between the PET index, clinical progression, and the UPDRS.

The paper gives little detail about how the UPDRS was administered, presumably only once, before each of the two PET scans an average of 18 months apart. A linear regression was then applied to the mean of each patient's two UPDRS and PET assessments, the gradient of which was expressed as a percentage change in the PET index for a change of 10 points "in the total UPDRS".

Some questions can be raised:

(1) Did the same observer administer the UPDRS blinded to the clinical diagnosis, on their 16 normal controls as well as to each patient on both occasions and, if not, was interobserver reliability studied?

(2) Presumably the "total UPDRS", judging by the scale shown on their figure A, was actually the total score from the 14 items in the motor subset of the UPDRS, which measures impairment rather than disability.

(3) The UPDRS is neither a perfect nor a linear scale. Indeed two coauthors of this paper have pointed out elsewhere the low interrater reliability in some items and redundancy in others.[2] It is a composite multi-item index of severity of disease, each item being an ordinal rather than an interval 0–4 scale of one clinical feature. The key distinction is that an ordinal scale permits the recording of data in rank order (for example, mild, moderate, severe) but without uniform intervals. Thus tremor score 4 is not twice as bad as 2, still less a total motor UPDRS score of 40/70 *v* 20/70. For these reasons, the use of simple arithmetic means as well as other parametric statistical methods is inappropriate, however tempting.

One illustration of the non-linearity of the UPDRS manifest to anyone who has used it regularly in clinical trials is the bias towards intermediate scores. Those with advanced disease and high scores are seldom if ever recruited, and some of the items scored as 1, indicating slight or mild impairment, "could be normal for some" according to the definition. In one study of Alzheimer's disease, 56% of 78 cases and 12 of the 20 age matched controls were found to have isolated extrapyramidal signs with motor UPDRS scores of 4.5 (± 4.8) and 2.8 (± 1.8) respectively using observers not blinded to the diagnosis.[3] It would be interesting to know whether a UPDRS score>0 is sensitive to or predictive of preclinical parkinsonism and/or abnormal PET.

Furthermore, as it is acknowledged that Parkinson's disease may progress at varying rates between patients and possibly within the same patient at different ages and stages, it is perhaps not surprising that the authors found no significant correlation between change in UPDRS and change in any PET index over 18 months. Thus it seems unwise to draw such firm conclusions based on the assumption that both measures are linear and directly correlated.

RICHARD J HARDIE
St George's Healthcare, Wolfson Neuro-rehabilitation Centre, Regional Neurosciences Unit, Atkinson Morley's Hospital, Copse Hill, Wimbledon, London SW20 0NE, UK.

1 Morrish P, Rakshi JS, Bailey DL, *et al*. Measuring the rate of progression and estimating the preclinical period of Parkinson's disease with [^{18}F] dopa PET. *J Neurol Neurosurg Psychiatry* 1998;**64**:314–19.
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Morrish replies:

We thank Hardie for his comments but are surprised that he finds difficulty in our assumption of a relation between PET index, clinical progression, and the UPDRS. Whether clinical severity is measured by UPDRS, bradykinesia scores, rigidity scores or Purdue pegboard scores[1 2] such a relation has been a consistent finding in [18F]dopa PET imaging studies of Parkinson's disease. The UPDRS was administered on 57 of 64 occasions by one observer (PKM) and on seven occasions by a second observer (JSR). UPDRS scoring was not carried out on the normal volunteers. Gonera *et al* have identified some non-specific symptoms that may predate the development of Parkinson's disease[3] but we know of no population study of the predictive value of UPDRS score in normal subjects. By total UPDRS score we mean the combined scores of sections I, II, III, and IV. Similar results were found when motor scores alone were examined.[4] The UPDRS scale is the most widely used index of global disease severity in Parkinson's disease. We accept that a linear correlation between UPDRS and PET index may have been inappropriate. The PET index represents a figure of mean [18F] dopa metabolism throughout the putamen, caudate, or total striatum whereas the clinical presentation and severity of parkinsonism is likely to depend on the distribution and severity of loss of dopaminergic function (and that of other neurotransmitters) within and outside the basal ganglia. It is unlikely that the relation is so simple yet this approach has allowed the demonstration of an aspect of the measurement of progression by PET that has not previously been considered, that of sensitivity to clinical severity. It should be noted that this discussion is not relevant to the major findings of the study (that measurement of progression is dependent on the PET method and that the average preclinical period is likely to be short), only to our explanation of these findings. However, it does suggest an important debate; should clinical indices or functional imaging indices be used independently in studies of progression in Parkinson's disease? When the reproducibility of both measurements is taken into account it is, as Hardie comments, not surprising that we found no significant correlation between change in UPDRS and change in PET index.

PAUL MORRISH
Department of Neurology, University Hospital of Wales, Heath Park, Cardiff CF4 4XN, UK

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Utilisation and costs of profession care and assistance according to disability of patients with multiple sclerosis in Flanders (Belgium)

In their detailed cost of illness study, Carton *et al* estimate the total annual costs in their population of 5500 people with multiple sclerosis to be ECU 13 106 000 (£8.7m) for ambulatory care and ECU 26 581 000 (£17.7m) for hospital and institutional care.[1]

They have adopted a "bottom up" approach which allows costs to be identified for different levels of disability, a distinct advantage from previous "top down" costs of illness studies.[2 3]

They conclude, as have others,[4] that the costs of multiple sclerosis rise with increasing disability and that the information is useful for cost effectiveness studies.

However, to be useful for such studies, the costs would need further description, in particular we would need to know which costs were fixed, and which were semifixed or nonfixed. In our own institution we know that 40% of the cost of a bed-day is fixed and at most 5% of costs are non-fixed. The remaining costs are semifixed—for example, staff salaries (Robert Hudson, Scottish Health Purchasing Information Centre, personal communication January 1998). The important point is that most of the costs in their paper are probably fixed or semifixed, and interventions to reduce disability are unlikely to have a significant impact on these costs as